

Serial No.: 09/334,969
Group Art Unit: 1644
Examiner: M. DiBrino

COPY OF PAPERS
ORIGINALLY FILED

RECEIVED

AUG 28 2002

TECH CENTER 1600/2900

CLAIMS AS CURRENTLY PENDING

SERIAL NO. 09/334,969

Filed June 17, 1999

~~July 17, 2001~~

1. (Amended) A synthetic multivalent T cell receptor (TCR) complex for binding to a MHC-peptide complex, which TCR complex comprises a plurality of T cell receptors specific for the MHC-peptide complex, wherein each TCR in the complex is a refolded recombinant TCR which comprises:

- F¹
- i.) a recombinant TCR α or γ chain extracellular domain having a first C-terminal dimerization peptide which is heterologous to the α or γ chain; and
 - ii.) a recombinant TCR β or δ chain extracellular domain having a second C-terminal dimerization peptide which is specifically heterodimerized with the first heterodimerization peptide to form a heterodimerization domain,

wherein a disulfide bond present in native TCRs between the α and β or γ and δ chains adjacent to the cytoplasmic domain is absent from the recombinant TCR.

2. The TCR complex according to claim 1, wherein the T cell receptors are $\alpha\beta$ T cell receptors having an α chain and a β chain.

3. The TCR complex according to claim 2, wherein the α chain and β chain are soluble forms of T cell receptor α and β chains.

F² 4. (Amended) The TCR complex according to claim 1, wherein the T cell receptors are in the form of multimers of two or more T cell receptors.

5. The TCR complex according to claim 4, wherein the multimer is a trimer or a tetramer.

6. (Amended) The TCR complex according to claim 1, wherein the T cell receptors are associated with one another via a linker molecule.

F³ 7. (Amended) The TCR complex according to claim 6, wherein the linker molecule is a multivalent attachment molecule.

F3
Cancel
8. (Amended) The TCR complex according to claim 7, wherein at least one of the T cell receptor α or β chains is derived from a fusion protein comprising an amino acid sequence encoding a protein tag.

9. The TCR complex according to claim 8, wherein the T cell receptors are biotinylated.

F4
10. (Twice Amended) The TCR complex according to claim 1, comprising a multimerized recombinant T cell receptor heterodimer having enhanced binding capability compared to a non-multimeric T cell receptor heterodimer.

F5
11. (Amended) A multivalent TCR complex comprising a multimerized recombinant T cell receptor heterodimer having enhanced binding capability compared to a non-multimeric T cell receptor heterodimer, wherein each TCR in the complex is a refolded recombinant TCR which comprises:

- i) a recombinant TCR α or γ chain extracellular domain having a first C-terminal dimerization peptide which is heterologous to the α or γ chain; and
- ii) a recombinant TCR β or δ chain extracellular domain having a second C-terminal dimerization peptide which is specifically heterodimerized with the first dimerization peptide to form a heterodimerization domain,

wherein a disulfide bond present in native TCRs between the α and β or γ and δ chains adjacent to the cytoplasmic domain, is absent from the recombinant TCR.

F6
14. (Amended) The TCR complex according to claim 11, wherein the heterodimerization domain is a coiled coil domain.

15. (Amended) The TCR complex according to claim 14, wherein the dimerization peptides are c-jun and c-fos dimerization peptides.

F7
16. (Twice Amended) The TCR complex according to claim 11, comprising a flexible linker located between the T cell receptor chains and the heterodimerization peptides.

F8
17. (Amended) The TCR complex according to claim 1, wherein the T cell receptor is expressed in an *E. coli* expression system.

F8
conc
18. (Amended) The TCR complex according to claim 1, wherein the T cell receptor is biotinylated at the C-terminus.

19. (Amended) The TCR complex according to claim 1, wherein the T cell receptors are associated with a lipid bilayer.

20. The TCR complex according to claim 19, wherein the lipid bilayer forms a vesicle.

21. The TCR complex according to claim 20, wherein the T cell receptors are attached at the exterior of the vesicle.

22. (Amended) The TCR complex according to claim 20 or claim 21, wherein the T cell receptors are attached to the vesicle via derivatized lipid components of the vesicle.

23. (Amended) The TCR complex according to claim 19 or claim 20, wherein the T cell receptors are embedded in the lipid bilayer.

F9
24. (Twice Amended) The TCR complex according to claim 1, wherein the T cell receptors are attached to a solid structure.

25. (Amended) The TCR complex according to claim 1, further comprising a detectable label.

26. (Amended) The TCR complex according to claim 1, further comprising a therapeutic agent such as a cytotoxic agent or an immunostimulating agent.

27. (Amended) The TCR complex according to claim 1, in a pharmaceutically acceptable formulation for use *in vivo*.

R-126
³⁴
34. (New) The TCR complex according to claim 1, wherein the heterodimerization domain is a coiled coil domain.

³⁵
34. (New) The TCR complex according to claim ³⁴34, wherein the dimerization peptides are c-jun and c-fos dimerization peptides.

³⁶
25. (New) The TCR complex according to claim 1, comprising a flexible linker located between the T cell receptor chains and the heterodimerization peptides.